

MODULATION OF VASCULAR HEALING BY INHIBITION OF LEUKOCYTE ADHESION AND FUNCTION

Abstract of the Invention

Compounds that specifically inhibit or reduce leukocyte adhesion or function are useful to enhance vascular healing and lessen restenosis of blood vessels after revascularization, via angioplasty or bypass surgery, of diseased coronary, peripheral and cerebral arteries, and lessen stenosis or restenosis of surgically-placed bypass grafts and transplanted organs. Examples of these compounds are those which block cell surface integrins or their ligands, for example, the leukocyte integrin Mac-1 (CD11b/CD18, $\alpha M\beta 2$). As demonstrated by the examples, both superficial and deep injury was significantly reduced with treatment using an antibody to Mac-1 compared to both saline controls and IgG controls. After balloon angioplasty (superficial injury) neointimal area was reduced nearly 70%. The ratio of intimal:medial area, which is customarily used in balloon-injured experimental arteries to normalize for small normal variations in arterial size from one animal to another, was reduced over 75%. After endovascular stent implantation (deep injury) neointimal area was reduced nearly 40%. Extrapolated to humans, this reduction in the intimal thickening would reduce restenosis from occurring in approximately 30% of patients to less than 10% of patients.